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APPLICATION NO.	FILED DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/28/99	07/28/99	KAWABATA	7024

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ML EXAMINER

ART UNIT 646

PAPER NUMBER

06/14/01

DATE MAILED:

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/358,755

Applicant(s)

KAWABATA ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2001.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 10,12-18,20-23 and 43-71 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 and 20-23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 43-58 and 60-62 is/are allowed.
- 6) ☒ Claim(s) 10 and 63-71 is/are rejected.
- 7) ☒ Claim(s) 59 is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 18) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: \_\_\_\_\_



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## DETAILED ACTION

### *Continued Prosecution Application*

The request filed on 3/28/2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09358755 is acceptable and a CPA has been established. An action on the CPA follows.

### *Formal Matters*

Claims 1-2, 5-9, 11, 19 and 24-42 were cancelled, and new claims 43-71 were added in Paper No. 17, 3/28/2001. Claims 10, 12-18, 20-23 and 43-71 are pending. Claims 12-18, 20-23 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 10 and 43-71 are under consideration.

### *Response to Amendment*

The rejection to claims 1-11 and 19 under 35 USC § 112, first paragraph has been rendered moot by cancellation of the claims.

The rejection to claims 1-11 and 19 under 35 USC § 112, second paragraph has been rendered moot by cancellation of the claims.

The rejection to claim 11 under 35 USC § 102(b) has been rendered moot by cancellation of the claims.

The rejection to claim 19 under 35 USC § 103(a) has been rendered moot by cancellation of the claims.

***Claim Objections***

Claim 10 is objected to because of the following informalities: It is dependent on cancelled claim 2. Appropriate correction is required.

Claims 59 and 71 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The antisense oligonucleotide of claims 59 and 71 can be infringed without infringing the claims from which they depend.

Claim 62 is objected to because of the following informalities: There is a dash at the end of claim 62. Appropriate correction is required.

***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 63-71 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid consisting of SEQ ID NO: 2 and 3, does not reasonably provide enablement for nucleotide sequences which are "substantially the same as" nucleic acid sequences consisting of SEQ ID NO: 2 and 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 63 is overly broad in the recitation of "substantially the same as" since no guidance is provided as to which of the myriad of nucleic acid sequences encoding polypeptide species encompassed by the claim will retain the function of binding Transferrin. The specification provides insufficient guidance on expected performance parameters of any of the possible muteins of TfR2. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a TfR2 other than those exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is

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undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claim 63 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention. Claims 64-71 are rejected insofar as they depend on the recitation in claim 63 of "substantially the same as".

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim 10 encompasses chemical analogues of the nucleic acid encoding TfR2. These genres would appear to include sequences which encode functional TfR2 proteins. They may include fragments of TfR2, and other variants comprising deletions, substitutions, insertions, additions, or replacements of TfR2 sequences. Since there is no language describing functional limitations of the claimed sequences, the claimed nucleic acid sequences also include sequences which do not encode a functional TfR2 protein.

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing insufficient species within the

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genus. The specification provides a written description only for TfR polypeptide which is encoded by nucleic acids set forth in SEQ ID NO: 2 and 3.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 63-71 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 63 is vague and indefinite in the recitation of the term "substantially", which is a conditional term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific conditions supported by the specification which Applicant considers to be "substantial". Claims 64-71 are vague and indefinite insofar as they depend on the recitation of "substantial" in claim 63.

***Conclusion***

Claims 43-58, 60-62 are allowable.

Claims 10, 63-71 are rejected.

Claim 59 is objected to.



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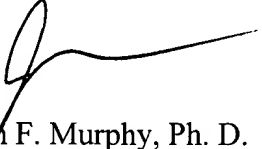
*Advisory Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245.

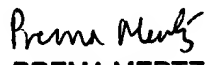
The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
June 6, 2001

  
PREMA MERTZ  
PRIMARY EXAMINER